ADVISORY COMMITTEE FOR PHARMACEUTICAL SCIENCE

November 28 - 29, 2001
CDER Advisory Committee Conference Room
5630 Fishers Lane
Rockville, MD

AGENDA

Day 2: Thursday, November 29, 2001

8:30 Call to Order — Vincent H. L. Lee, Ph.D., Acting Chair

Conflict of Interest — Nancy Chamberlin, Pharm.D., Exec.Sec.

8:45 **Dermatopharmacokinetics**

Introduction to the issues — Dale Conner, Pharm.D.
Director Div. Bioequiv. OGD

Data Presentations

9:15 Lynn Pershing, Ph.D., Univ. Utah

9:35 Thomas Franz, M.D., Oregon Health Science Univ.

9:55 Mamata Gokhale, Ph.D. Reviewer OGD

10:15 Introduction to discussion questions — Dale Conner, Pharm.D.
Director Div. Bioequiv. OGD

Committee Discussion

Invited Guests
Lloyd King, M.D., Derm. Consultant
Jonathan Wilkin, M.D., Director Div. Derm and Dental Products ORM
Leslie Benet, Ph.D., University of California, S.F.

Issue 1. Does the dermatopharmacokinetic (DPK) approach that studies drug disposition over time in the stratum corneum, provide a viable method for determining bioavailability and/or bioequivalence of topical dermatological products?

Issue 2. To be suitable as a regulatory method, a technique should provide similar conclusions between laboratories that are experienced at performing the method. Does the DPK approach show an appropriate level of between-lab consistency?

Issue 3. Ideally, a regulatory method should not be so difficult or complex that it can only be performed by one or two experts in the field. Is DPK a method that can be set up in any testing laboratory? What is the time, effort and cost involved in setting up this technique so that the method can be properly validated and performed?

10:45 Break

11:00 Open Public Hearing

12:00 Lunch

1:00 **Individual Bioequivalence**

	Introduction to the topic and discussion topics	Lawrence Lesko, Ph.D. Director, OCBP
1:15	Background and Concepts of Individual Bioequivalence	Mei-Ling Chen, Ph.D. Assoc. Dir. Quality Implementation - Biopharm.
1:30	Results from Replicate Design Studies in NDA's and FDA database	Mei-Ling Chen, Ph.D. Assoc. Dir. Quality Implementation - Biopharm
1:45	Results from Replicate Design Studies in ANDA's	Rabi Patnaik, Ph.D. Dep. Director Div. Bioequiv. OGD
2:00	Individual Bioequivalence:Have the opinions of the scientific community changed?	Leslie Benet, Ph.D. University of California, S.F.
2:15	FDA Research Plan	Stella Machado, Ph.D. Director, QMR Staff ORM

2:30 Break

2:45 **Individual Bioequivalence - continued**

Discussion by Committee Members and
Invited Guests:
Sandy Bolton, Ph.D.
Lazlo Endrenyi, Ph.D., Univ. Toronto
Nevine Zariffa, Ph.D., GlaxoSmithKline Pharmaceuticals
Avi Yacobi, Ph.D., Taro Pharmaceuticals
Leslie Benet, Ph.D., University of California, S.F.

Discussion Topic 1

Is it reasonable and appropriate for FDA to use average bioequivalence (ABE) for market access, unless there is a compelling reason not to, for an interim period of another year until a final decision is made to use individual bioequivalence (IBE) for market access?

Discussion Topic 2

The Advisory Committee is asked to comment on the proposal that if the FDA were to use IBE for market access (when there is a compelling reason not to use ABE) during the interim period, the following conditions would apply (below).

-- The sponsor declares IBE for data analysis a priori in BE study protocol
-- A heterogeneous population is enrolled in the study
-- The mean Test/Reference ratio is constrained to +/- 15%
-- There are no significant subject-by-formulation interaction, SxF (> 0.15)
-- The study includes at least 24 subjects
-- The study passes the IBE criterion

Discussion Topic 3

Are there scientific, technical or other reasons not to continue with the recommendations in the General BA/BE Guidance to a) conduct replicate design studies for modified release dosage forms and for highly variable drugs, and b) to use a heterogeneous study population (at least 40% male and female subjects, and/or young and elderly subjects)?

Discussion Topic 4

The Advisory Committee is asked to comment on plans for further research programs and projects associated with the use of ABE and IBE to allow comparison of bioavailability measures and to arrive at a final conclusion and recommendation on IBE.

4:30 Adjourn